

In Vivo Iontophoretic Delivery of Salmon Calcitonin across Microporated Skin

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Purpose: To determine the effect of iontophoresis and its combination with microneedles on the in vivo delivery of salmon calcitonin (SCT) as a model peptide.

Methods: Microneedles, iontophoresis and the combination were investigated for their effect on the transdermal delivery of SCT in vivo using the hairless rat. SCT (350 µl of a 1 mg/ml solution in 50mM citrate buffer, pH 4.0) was placed in a cartridge designed for iontophoresis. Maltose microneedles (500 micron, Texmac Inc.), stacked in three layers, were used to porate the skin prior to the application of the drug with or without iontophoresis. Since SCT (pI 10.4) was positively charged at pH 4, constant current iontophoresis (0.2mA/cm², 1 hr) was conducted with the anode connected to the cartridge, and the cathode connected to a TransQ (IOMED, Inc.) inactive electrode. Transport of drug across the skin was assessed by collecting blood samples at regular intervals via the tail vein which were analyzed for serum SCT using ELISA.

Results:

The maximum concentrations of SCT in the serum were 41.45 pg/ml, 605.21 pg/ml, and 2374.06 pg/ml under microneedles alone, 1 hr iontophoresis alone, and the combination, respectively. When compared to the delivery with microneedles alone, the increase in concentration with iontophoresis alone was 15-fold ($p < 0.05$) and with the combination of microneedles the increase was 57-fold ($p < 0.05$). The total amount of SCT delivered by iontophoresis and its combination with microneedles in the hairless rat was 648.67 ng/kg and 3075.96 ng/kg, respectively, as calculated by WinNonlin.

Conclusion: Iontophoresis or a disruption of the skin barrier by microneedles enabled the transdermal delivery of SCT. A combination of iontophoresis and microneedles resulted in the highest delivery flux.

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